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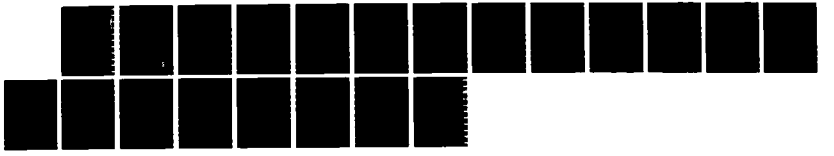

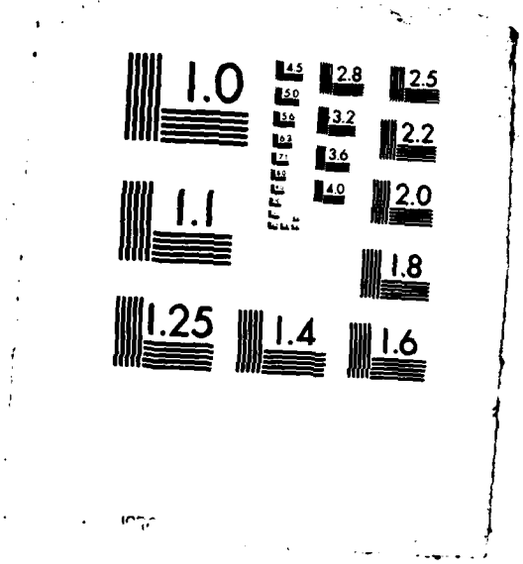
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Exact Significance Testing with Biased Coin Randomization

by

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Key Words: Biased coin design; Censoring; Complete randomization; Conditional randomization distribution; Markov chain; Randomization test.

Exact Significance Testing with Biased Coin Randomization

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Abstract

For a clinical trial where two treatments have been assigned sequentially to the patients via Efron's (1971) biased coin design, a recursion procedure is derived for obtaining the exact randomization distribution of a class of test statistics. This enables one to perform exact significance tests of the hypothesis of no treatment difference. The randomization distribution of the statistic is conditional on the imbalance of the treatment allocation. It is illustrated that if the analysis is performed as if complete randomization was used, conservative and anticonservative errors can be incurred. The applicability of the test to censored data is also discussed.

1. INTRODUCTION

In clinical trials to compare the efficacy of treatments A and B, patients typically arrive sequentially and upon arrival are assigned a treatment or otherwise excluded from the trial. Several designs are possible for assigning the treatments. Complete randomization assigns treatments on the basis of the outcomes of independent tosses of a fair coin, whereas systematic design alternately assigns the treatments after the first patient has been assigned a treatment. The complete randomization design is optimal in minimizing selection bias (see Blackwell and Hodges, 1957), the bias introduced when the experimenter can predict with high probability the treatment an incoming patient will receive. It also controls accidental bias, the effect of covariates, time trends, etc., on the statistical analysis of the resulting data. However it suffers from the defect that it could produce highly imbalanced treatment allocations especially for small-sample trials (Efron 1971 and Pocock 1979). Such an imbalance may decrease the efficiency of statistical procedures, and may also lead to less credible results (Halpern and Brown 1986; Smith 1984b). In contrast, the systematic design is optimal in balancing the treatment allocation, but is the worst design in controlling selection and accidental bias.

Efron (1971) introduced the biased coin design with bias p, abbreviated BCD(p) for convenience. This design is a compromise between the complete randomization and systematic designs. Let $T_1, T_2, \ldots$ denote the sequence of assignment variables with $T_i = 0$ or 1 according to whether the i^{th} patient receives treatment A or B, respectively. With $D_0 = 0$, define for $i = 1, 2, \ldots$

$$D_i = 2 \sum_{j=1}^{i} T_j - i . \qquad (1.1)$$

Under the BCD(p) where $0.5 < p < 1$, the probability that the $(i+1)^{th}$ patient receives B is p, 0.5 or $q = 1 - p$ depending on whether $D_i <$, $=$, or > 0, respectively. Wei(1977, 1978) generalized this by allowing the assignment probabilities for the $(i+1)^{th}$ patient to depend both on i and D_i. Efron (1971), Wei (1977, 1978) and Smith (1984a, b) demonstrated that these designs compare quite well with complete randomization in controlling selection and accidental bias in addition to having better balancing properties.

We confine our attention to a clinical trial where treatments A and B have been assigned to n patients via the BCD(p), and study the randomization test of H_0, the null hypothesis of no treatment difference. We consider test statistics of the form

$$S_n = \sum_{i=1}^{n} a_i T_i , \qquad (1.2)$$

so that the two-sided version of the randomization test rejects H_0 whenever S_n is either "too small" or "too large." In (1.2), $a_1, \ldots, a_n$ is a nonrandom sequence of scores associated with the sequence of patient responses $x_1, \ldots, x_n$, and these scores are typically functions of the ranks of the x_i's. In deciding whether S_n is too small or too large, Cox(1982) suggested taking the randomization distribution of S_n over those treatment allocations with the same or nearly the same terminal imbalance as the observed allocation. In accordance with this suggestion, our results are conditional on D_n, the terminal imbalance of the treatment allocation.

In Section 2 we utilize the Markovian structure of $D_0, D_1, \ldots$ to derive a recursion procedure for obtaining the exact distribution of S_n, conditional on $D_n = m$. This procedure enables one to perform exact significance tests of H_0. In Section 3 we present procedures for computing higher-order probabilities of $D_0, D_1, \ldots$ and suggest possible approximations. These probabilities are

needed in the recursion of Section 2. Section 4 illustrates the consequences of ignoring the BCD(p) allocation and instead acting as if complete randomization was used; while Section 5 considers the applicability of the randomization test to censored patient responses.

Whereas our work focuses on exact results, previous research dealt mostly with asymptotic results. Efron (1971) presented an asymptotic argument showing that if one ignores the BCD(p) allocation and instead acts as if complete randomization was used, the randomization test of H_0 could be conservative or anticonservative. Halpern and Brown (1986) concluded on the basis of their simulation results that in the case where the patient responses are binary, the classical 2×2 χ^2-test should not be used to compute significance probabilities when the observed responses exhibit a strong trend. Smythe and Wei (1983) derived the asymptotic null distribution of S_n under Wei's (1977) urn design. Cox (1982) and Smith (1984b) discussed the randomization tests of H_0 for special cases of Wei's (1978) biased coin designs. Wei, Smythe and Smith (1986) derived the asymptotic null distribution of the k-treatment version of (1.2) when the treatments are assigned via a k-treatment version of Wei's biased coin design.

2. THE RANDOMIZATION DISTRIBUTION

Let $\underset{\sim}{Z}$ denote the set of integers, $\underset{\sim}{Z}_+$ the set of positive integers, and set $\underset{\sim}{Z}_+^0 = \underset{\sim}{Z}_+ \cup \{0\}$. By the defining property of the BCD(p), the process $D_0, D_1, \ldots,$ in (1.1) is a homogeneous Markov chain with state space $\underset{\sim}{Z}$. It has stationary transition probabilities

$$P_{i,j} = \Pr(D_1=j \mid D_0=i), \qquad j \in \underset{\sim}{Z},\ i \in \underset{\sim}{Z}$$

$$= \begin{cases} .5 & \text{if } j = \pm 1,\ i = 0 \\ p & \text{if } (j=i+1,\ i<0) \text{ or } (j=i-1,\ i>0) \\ q & \text{if } (j=i-1,\ i<0) \text{ or } (j=i+1,\ i>0) \\ 0 & \text{otherwise.} \end{cases} \tag{2.1}$$

Let $\{P^n_{i,j}: i \in \underset{\sim}{Z}, j \in \underset{\sim}{Z}\}$ be the n^{th} order transition probabilities of this chain, and represent the randomization distribution of S_n, given $D_n = m$, by

$$h^n_m(s) = \begin{cases} \Pr\{S_n=s \mid D_0=0, D_n=m\}, & s \in \Delta^n_m,\ P^n_{0,m} > 0 \\ 0 & \text{otherwise} \end{cases}$$

where

$$\Delta^n_m = \{ \sum_{i=1}^{n} a_i t_i : t_i \in \{0,1\} \text{ and } 2 \sum_{i=1}^{n} t_i - n = m \}.$$

Then we have the following procedure for computing $\{h^n_m(s)\}$. For continuity of presentation, proofs of the theorems are deferred to the Appendix.

Theorem 1. If $m \in \underset{\sim}{Z}$ with $P^n_{0,m} > 0$ and $s \in \Delta^n_m$, then

$$h^n_m(s) = (P^n_{0,m})^{-1} J^n_m(s),$$

where $\{J^k_m(s)\}$ satisfy the recursion equation

$$J^k_m(s) = \gamma_{m-1} J^{k-1}_{m-1}(s-a_k) + (1-\gamma_{m+1}) J^{k-1}_{m+1}(s), \quad k = 1, \ldots, n,$$

with initial and boundary conditions $J^0_m(s) = 1$ if $m = 0$ and $s = 0$, 0 otherwise; and where $\gamma_m = p, .5, q$ according to whether $m <, =, > 0$, respectively.

An immediate consequence of this theorem is

$$P^n_{0,m} = \sum_u J^n_m(u) \tag{2.2}$$

where $\sum_u$ denotes summation over all $u \in \Delta^n_m$. Combined with Theorem 1 this shows that

$$h^n_m(s) = \{\sum_u J^n_m(u)\}^{-1} J^n_m(s), \qquad s \in \Delta^n_m.$$

Using (2.2) to obtain $P^n_{0,m}$ requires knowledge of $J^n_m(u)$ for all $u \in \Delta^n_m$. But to compute significance probabilities one usually needs only those values of $h^n_m(u)$ and $J^n_m(u)$ for u beyond the observed value of S_n. In Section 3 we therefore present a different method for computing $P^n_{0,m}$ which does not require knowledge of $\{J^n_m(u)\}$.

The next result allows us to restrict attention to conditional randomization distributions with $D_n = m \geq 0$.

Theorem 2. If $m \in \underset{\sim}{Z}^0_+$ with $P^n_{0,m} > 0$ and $s \in \Delta^n_m$, then $h^n_m(s) = h^n_{-m}(\sum_{i=1}^n a_i - s)$.

Observe that when $a_i = \text{rank}(x_i)$ the recursion in Theorem 1 has some similarity with that of Mann and Whitney (1947) for the Mann-Whitney-Wilcoxon U statistic. However, in contrast to the distribution of U, $\{h^n_m(s)\}$ is not invariant with respect to permutations of the scores $a_1, \ldots, a_n$. This is illustrated by Table 1 which summarizes the conditional randomization distribution of S_n, under BCD(2/3), for all permutations of the ranks. (For economy of space we just list the distributions for $n = 4$ and $m = 0$.)

Table 1. Randomization Distributions of S_n for the 24 Rank Permutatinns under BCD(2/3) with n = 4 and m = 0.

Rank Sequences				Values of S_n				
				3	4	5	6	7
1234	1243	2134	2143	$\frac{2}{16}$	$\frac{3}{16}$	$\frac{6}{16}$	$\frac{3}{16}$	$\frac{2}{16}$
4321	3421	4312	3412					
1324	1342	3124	3142	$\frac{3}{16}$	$\frac{2}{16}$	$\frac{6}{16}$	$\frac{2}{16}$	$\frac{3}{16}$
4231	2431	4213	2413					
1423	1432	4123	4132	$\frac{3}{16}$	$\frac{3}{16}$	$\frac{4}{16}$	$\frac{3}{16}$	$\frac{3}{16}$
3241	2341	3214	2314					

We developed a FORTRAN subroutine that implements the recursion procedure in Theorem 1 for the case $a_i = \text{rank}(x_i)$ and $D_n = m \geq 0$. Interested readers could obtain this program by writing to Edsel Peña. Using the Cyber 730 computer, the computer time required by this program to obtain the conditional randomization distribution of S_n for n = 6, 12, 18, 24 and 30 with m = 0 and p = 2/3 were 0.15, 0.81, 3.16, 9.14 and 20.75 CPU seconds, respectively. Note the exponential rate of increase of the time as n increases. In a forthcoming report, we present large-sample approximations that enables one to obtain approximate p-values when the recursion in Theorem 1 is not practically feasible.

3. HIGHER-ORDER PROBABILITIES

We now present recursive methods for computing the higher-order transition probabilities of the process $D_0, D_1, \ldots$. Let $Y_1, Y_2, \ldots$ be identically distributed and independent random variables with $Pr(Y_1=1) = q = 1 - Pr(Y_1=-1)$.

With $W_0 = 0$, define $W_i = Y_1 + \ldots + Y_i$ for $i \in \underset{\sim}{Z}_+$. The process $W_0, W_1, \ldots$ is the unsymmetric random walk with negative drift. For $j \in \underset{\sim}{Z}_+^0$ and $n \in \underset{\sim}{Z}_+$, let

$$f_{0,j}^n \equiv \Pr\{\bigcap_{i=1}^{n-1}(D_i \neq j);\ D_n = j \mid D_0 = 0\},$$

$$b_{0,j}^n \equiv \Pr\{\bigcap_{i=1}^{n-1}(W_i \geq 0);\ W_n = j \mid W_0 = 0\}.$$

Furthermore, let C(b,a) denote the number of combinations of a items taken from b items.

Then the higher-order transition probabilities satisfy the following:

Theorem 3. For $n \in \underset{\sim}{Z}_+$ and $m \in \underset{\sim}{Z}_+$,

(i) $$P_{0,0}^n = \sum_{k=1}^{n} f_{0,0}^k \, P_{0,0}^{n-k},$$

(ii) $$P_{0,m}^n = (.5)b_{0,m-1}^{n-1} + \sum_{k=1}^{n} f_{0,0}^k \, P_{0,m}^{n-k}.$$

Theorem 4.

(i) $f_{0,0}^{2n-1} = 0$ and $f_{0,0}^{2n} = (2n-1)^{-1} \, C(2n-1,n-1) p^n q^{n-1}$ for $n \in \underset{\sim}{Z}_+$,

(ii) $b_{0,m}^n = \{(m+1)/(n+1)\} \, C(n+1,(n+m+2)/2) p^{(n-m)/2} \, q^{(n+m)/2}$

for $n \in \underset{\sim}{Z}_+^0$, $m \in \underset{\sim}{Z}_+^0$.

Efron (1971) obtained the stationary distribution of $|D_0|, |D_1|, \ldots$. From this distribution, the stationary distribution probabilities of $D_0, D_1, \ldots$ denoted by $\{\pi_j, j \in \underset{\sim}{Z}\}$ are found to be

$$\pi_0 = (p-q)/(2p) \text{ and } \pi_j = \pi_{-j} = (p-q)/(4p^2)(q/p)^{j-1}, \quad j \in \underset{\sim}{Z}_+.$$

Since $D_0, D_1, \ldots$ has period 2 it follows that the limiting values of $P^{2n}_{0,2m}$ and $P^{2n-1}_{0,2m-1}$ are $2\pi_{2m}$ and $2\pi_{2m-1}$, respectively. For large n we could approximate $P^n_{0,m}$ in Theorem 1 by these limiting values. Computations show that these approximations are quite good for sample sizes of at least 30. This is illustrated by Table 2 which summarizes the exact values of $P^n_{0,m}$ for $6 \le n \le 30$ and $0 \le m \le 6$ under BCD(2/3). These values were computed using Theorems 3 and 4. The last row contains the limiting probabilities. Notice the close agreement between $P^{30}_{0,m}$ and $2\pi_m$ when m is even, and $P^{29}_{0,m}$ and $2\pi_m$ when n is odd.

4. A SIMULATION STUDY

A computer simulation was performed to illustrate the consequences of ignoring the BCD(p) allocation and instead acting as if complete randomization was used. This simulation was done on a Cyber 730 computer at the Florida State University Computing Center. The uniform random number generator used was the intrinsic routine RANF.

Five hundred replicates were generated of the following experiment. Each experiment consisted of generating $n = 15$ independent uniform (0,1) variates $x_1, \ldots, x_{15}$ and obtaining their associated ranks $a_1, \ldots, a_{15}$, and then generating the treatment assignment variates $t_1, \ldots, t_{15}$ via the BCD(2/3). After stratifying these 500 replicates according to their value of $D_{15} = m$, the conditional randomization distributions $\{h^{15}_m(s)\}$ were obtained using the FORTRAN program mentioned in Section 2. For each of these distributions, the α-level conservative critical values s_0 corresponding to the one-sided test which rejects H_0 when S_{15} is small was determined. The significance levels were set to 0.01, 0.05 and 0.10. Note that s_0 is conservative in the sense that $\Pr(S_{15} \le s_0 | D_0 = 0, D_{15} = m) \le \alpha$ and $\Pr(S_{15} \le s_0 + 1 | D_0 = 0, D_{15} = m) > \alpha$.

Table 2. Exact Higher-Order Transition ($P^{n}_{0,m}$) and Limiting ($2\pi_m$) Probabilities of D_0, D_1, ... under BCD(2/3).

n	m						
	0	1	2	3	4	5	6
6	0.5597		0.1893		0.0288		0.0021
7		0.4060		0.0823		0.0110	
8	0.5413		0.1902		0.0347		0.0041
9		0.3975		0.0866		0.0143	
10	0.5300		0.1902		0.0384		0.0058
11		0.3918		0.0890		0.0167	
12	0.5224		0.1899		0.0408		0.0071
13		0.3878		0.0905		0.0183	
14	0.5171		0.1896		0.0424		0.0081
15		0.3850		0.0915		0.0195	
16	0.5133		0.1893		0.0435		0.0088
17		0.3828		0.0921		0.0204	
18	0.5104		0.1890		0.0443		0.0094
19		0.3812		0.0925		0.0211	
20	0.5083		0.1888		0.0449		0.0099
21		0.3800		0.0928		0.0216	
22	0.5067		0.1886		0.0453		0.0102
23		0.3790		0.0931		0.0219	
24	0.5054		0.1884		0.0456		0.0105
25		0.3783		0.0932		0.0222	
26	0.5044		0.1882		0.0459		0.0107
27		0.3777		0.0933		0.0225	
28	0.5036		0.1881		0.0461		0.0109
29		0.3772		0.0934		0.0226	
30	0.5029		0.1880		0.0462		0.0110
$2\pi_m$	0.5000	0.3750	0.1875	0.0937	0.0468	0.0234	0.0117

Table 3 is a summary of the results of this simulation. The second column shows the number of replicates that have $D_{15} = m$. The last three pairs of columns show the percentages of replicates, for each value of m, that have α-level critical value s_0. We excluded the cases $m = -5$ and $m = 5$ since there were only 15 and 9 replicates in each, respectively. Those values of s_0 that are superscripted by an asterisk are the α-level critical values under complete randomization.

Table 3 shows that if one ignores the BCD(p) allocation and instead performs the randomization test employing the critical value derived under complete randomization, the test could be conservative or anticonservative. Conservatism is illustrated by the cases $m = -1$ and $m = 1$ with $\alpha = 0.01$, while the latter is manifested by the cases $m = -1$ and $m = 1$ with $\alpha = 0.05$ and $\alpha = 0.10$.

5. APPLICABILITY TO CENSORED DATA

The simulation study in the preceding section dealt only with uncensored responses. However, the test discussed here can also accomodate censored data, albeit from a more restricted censorship model than is typically assumed. Let $X_1, \ldots, X_n$ be the independent response variables of the patients, and $Y_1, \ldots, Y_n$ be the sequence of independent censoring variables, with the $\{X_i\}$ independent of the $\{Y_i\}$. In the typical nonparametric two-sample censorship model it is assumed that Y_i conditional on $T_i = 0$ has distribution G_1, and Y_i conditional on $T_i = 1$ has distribution G_2, where G_1 and G_2 are unspecified. For our randomization test to be valid in this censored situation, we need to impose the requirement that $G_1 = G_2$. (This "equal censoring distribution" restriction may

Table 3. Number of Replicates With $D_{15} = m$, and Percentages of Replicates For Each Value of m with α-Level Critical Value s_0.

m	No. of Replicates	α = 0.01		α = 0.05		α = 0.10	
		s_0	%	s_0	%	s_0	%
-3	56	26	5.36	31	3.57	34	5.36
		27	28.57	32	25.00	35	25.00
		28*	35.71	33*	39.29	36*	39.29
		29	23.21	34	23.21	37	23.21
		30	7.14	35	8.93	38	7.14
-1	178	34	10.11	39	1.12	42	1.12
		35*	43.82	40	40.45	43	42.70
		36	34.27	41*	43.26	44*	40.45
		37	10.67	42	12.92	45	14.04
		38	1.12	43	2.25	46	1.69
1	202	42	8.91	47	1.49	50	0.50
		43*	39.60	48	34.16	51	37.13
		44	37.62	49*	42.57	52*	40.59
		45	12.87	50	18.81	53	18.81
		46	0.50	51	2.48	54	2.48
		47	0.50	52	0.50	55	0.50
3	36	50	5.56	55	5.56	58	5.56
		51	36.11	56	30.56	59	33.33
		52*	44.44	57*	47.22	60*	44.44
		53	8.33	58	8.33	61	8.33
		54	5.56	59	8.33	62	8.33

*Critical values under complete randomization.

not be unreasonable in clinical trials where patient arrival and treatment assignment is sequential.) Under this restriction, the test could then make use of a wide variety of choices for the a's. For example, Gehan's (1965) method of assigning the scores is as follows: Let $(Z_1,\delta_1), \ldots, (Z_n,\delta_n)$ be the observed censored data where $Z_i = \min(X_i,Y_i)$ and $\delta_i = I(X_i \le Y_i)$. For $i,j = 1, \ldots, n$, define

$$\eta_{ij} = \begin{cases} 0 & \text{if} \quad (Z_i \le Z_j,\ \delta_i=1) \\ 0.5 & \text{if} \quad (Z_i \le Z_j,\ \delta_i=0) \text{ or } (Z_i > Z_j,\ \delta_j=0) \\ 1 & \text{if} \quad (Z_i > Z_j,\ \delta_j=1). \end{cases}$$

The Gehan scores are obtained by letting $a_i = 1 + \sum_{i \ne j} \eta_{ij}$, $i = 1, \ldots, n$.

APPENDIX: PROOFS

Proof of Theorem 1. Let $m \in \underset{\sim}{Z}$ with $P^n_{0,m} > 0$ and $s \in \Delta^n_m$. Then

$$\begin{aligned} h^n_m(s) &= \Pr(S_n=s, D_{n-1}=m-1 \mid D_0=0, D_n=m) + \Pr(S_n=s, D_{n-1}=m+1 \mid D_0=0, D_n=m) \\ &= \Pr(S_{n-1}=s-a_n, D_{n-1}=m-1 \mid D_0=0, D_n=m) + \Pr(S_{n-1}=s, D_{n-1}=m+1 \mid D_0=0, D_n=m) \\ &= \Pr(D_{n-1}=m-1 \mid D_0=0, D_n=m) \Pr(S_{n-1}=s-a_n \mid D_0=0, D_{n-1}=m-1, D_n=m) \\ &\quad + \Pr(D_{n-1}=m+1 \mid D_0=0, D_n=m) \Pr(S_{n-1}=s \mid D_0=0, D_{n-1}=m+1, D_n=m). \end{aligned}$$

Conditional on D_{n-1}, S_{n-1} and D_n are independent by the Markov property of $D_0, D_1, \ldots, D_n$. Furthermore, $\Pr(D_{n-1}=m-1 \mid D_0=0, D_n=m) = P^{n-1}_{0,m-1}\,\gamma_{m-1}/P^n_{0,m}$ and $\Pr(D_{n-1}=m+1 \mid D_0=0, D_n=m) = P^{n-1}_{0,m+1}(1-\gamma_{m+1})/P^n_{0,m}$. Therefore,

$P^n_{0,m}h^n_m(s) = \gamma_{m-1}P^{n-1}_{0,m-1}h^{n-1}_{m-1}(s-a_n) + (1-\gamma_{m+1})P^{n-1}_{0,m+1}h^{n-1}_{m+1}(s)$. Letting $J^k_m(s) = P^k_{0,m}h^k_m(s)$ we obtain the recursion equation for $\{J^k_m(s)\}$. The initial and boundary conditions follow from the fact that $h^0_m(s) = 1$ if $m = 0$ and $s = 0$, 0 otherwise, and $P^0_{0,m} = 1$ if $m = 0$, 0 otherwise.

Before proving Theorem 2 we first prove the following lemma.

Lemma 1. The process $D_0, D_1, \ldots$ is symmetric in the sense that

$$\Pr\{\bigcap_{i=1}^n (D_i=d_i) \mid D_0=d_0\} = \Pr\{\bigcap_{i=1}^n (D_i=-d_i) \mid D_0=-d_0\}$$

for every $d_0, \ldots, d_n$ with $d_i \in \mathbb{Z}$.

Proof of Lemma 1. From (2.1) we obtain

$$\Pr(D_{i+1}=d_{i+1} \mid D_i=d_i) = \Pr(D_{i+1}=-d_{i+1} \mid D_i=-d_i).$$

By the Markov property of $\{D_k\}$ we have

$$\Pr\{\bigcap_{i=1}^n (D_i=d_i) \mid D_0=d_0\} = \prod_{i=1}^n \Pr(D_i=d_i \mid D_{i-1}=d_{i-1})$$

$$= \prod_{i=1}^n \Pr(D_i=-d_i \mid D_{i-1}=-d_{i-1}) = \Pr\{\bigcap_{i=1}^n (D_i=-d_i \mid D_0=-d_0\}. \quad \|$$

Corollary 1. $P^n_{i,j} = P^n_{-i,-j}$, $i \in \mathbb{Z}$, $j \in \mathbb{Z}$, $n \in \mathbb{Z}^0_+$.

Proof of Corollary 1. Follows from Lemma 1. $\|$

Proof of Theorem 2. Given $(t_1,\ldots,t_n)$ let $(t'_1,\ldots,t'_n) = (1-t_1,\ldots,1-t_n)$. Then $2\sum_{i=1}^n t_i - n = m$ and $\sum_{i=1}^n a_i t_i = s$ if and only if $2\sum_{i=1}^n t'_i - n = -m$ and $\sum_{i=1}^n a_i t'_i = \sum_{i=1}^n a_i - s$.

By Lemma 1 and Corollary 1 it follows that

$$\Pr\{\bigcap_{i=1}^n (T_i=t_i) \mid D_0=0, D_n=m\} = \Pr\{\bigcap_{i=1}^n (T_i=1-t_i) \mid D_0=0, D_n=-m\}.$$

Consequently, $h^n_m(s) = h^n_{-m}(\sum_{i=1}^n a_i - s)$. $\|$

Proof of Theorem 3. To prove (i) we have

$$P^n_{0,0} = \Pr[\bigcup_{k=1}^{n} \{\bigcap_{j=1}^{k-1}(D_j \neq 0);\ D_k=0, D_n=0\} | D_0=0]$$

$$= \sum_{k=1}^{n} \Pr\{\bigcap_{j=1}^{k-1}(D_j \neq 0);\ D_k=0 | D_0=0\} \Pr(D_n=0 | D_k=0)$$

using the Markov property of $\{D_k\}$. Since $\{D_k\}$ is homogeneous, (i) follows. For $m \in \mathbb{Z}_+$, we have

$$P^n_{0,m} = \Pr\{\bigcap_{i=1}^{n-1}(D_i>0);\ D_n=m | D_0=0\}$$

$$+ \Pr[\bigcup_{k=1}^{n} \{\bigcap_{i=1}^{k-1}(D_i \neq 0);\ D_k=0, D_n=m\} | D_0=0]$$

$$= (.5)\Pr\{\bigcap_{i=2}^{n-1}(D_i \geq 1);\ D_n=m | D_1=1\}$$

$$+ \sum_{k=1}^{n} \Pr\{\bigcap_{i=1}^{k-1}(D_i \neq 0);\ D_k=0 | D_0=0\} \Pr(D_n=m | D_k=0)$$

$$= (.5)\Pr\{\bigcap_{i=1}^{n-2}(W_i \geq 0);\ W_{n-1}=m-1 | W_0=0\} + \sum_{k=1}^{n} f^k_{0,0} P^{n-k}_{0,m}$$

since $D_1, D_2, \ldots$ is stochastically equivalent to $W_0, W_1, \ldots$ when $D_i \geq 1$ for $i = 1, 2, \ldots$, and $D_0, D_1, \ldots$ is homogeneous. Recalling the definition of $b^{n-1}_{0,m-1}$ we obtain (ii). ||

Proof of Theorem 4. That $f^{2n-1}_{0,0} = 0$ is immediate from the fact that $\{D_k\}$ is of period 2. On the otherhand,

$$f^{2n}_{0,0} = \Pr(D_1=1, D_2 \geq 1, \ldots, D_{2n-1} \geq 1, D_{2n}=0 | D_0=0)$$

$$+ \Pr(D_1=-1, D_2 \leq -1, \ldots, D_{2n-1} \leq -1, D_{2n}=0 | D_0=0).$$

By Lemma 1 these probabilities are equal, hence

$$f^{2n}_{0,0} = \Pr(D_2 \geq 1, \ldots, D_{2n-1} \geq 1, D_{2n}=0 | D_0=0, D_1=1)$$

$$= \Pr(W_1 > -1, \ldots, W_{2n-2} > -1, W_{2n-1} = -1 | W_0=0).$$

Each path from (0,0) to (2n-1,-1) must have probability $p^n q^{n-1}$ and by the ballot theorem (Feller 1968, p.66) there are $(2n-1)^{-1}C(2n-1,n-1)$ such paths, completing the proof of (i).

On the otherhand, each path from (0,0) to (n,m) has (n+m)/2 "up" steps and (n-m)/2 "down" steps, thus has probability $p^{(n-m)/2}q^{(n+m)/2}$. By the ballot theorem the number of paths from (0,0) to (n,m) lying above or on zero is $\{(m+1)/(n+1)\}\, C(n+1,(n+m+2)/2)$. Thus (ii) follows. ||

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